DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Rockville MD 20857

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Thomas J. Donegan, Jr.
Vice President-Legal & General Counsel
The Cosmetic, Toiletry, and Fragrance Association
1101 17th Street, N.W., Suite 300
Washington, D.C. 20036-4702

Re: Docket No. 78N-0038
Comment No. RPT 9

Dear Mr. Donegan:

This letter is in response to your submission dated April 9, 1996, and filed as Comment No. RPT 9 under Docket No. 78N-0038 in the Dockets Management Branch. This submission consists of a report from the Joint Sunscreen Task Force of The Cosmetic, Toiletry, and Fragrance Association (CTFA) and the Consumer Healthcare Products Association (CHPA) (formally the Nonprescription Drugs Manufacturers Association) on "Critical Wavelength Determination for the Evaluation of the UVA Efficacy of Sunscreen Products."

The report proposes a protocol for modification of the "Diffey method" for classifying the relative degree of ultraviolet A (UVA) protection of sunscreen drug products. In this protocol, critical wavelength (which is defined as the wavelength where the integral of the absorbance curve reaches 90 percent of the integral from 290 to 400 nanometers(nm)) is determined spectrophotometrically and used to support descriptive labeling. The absorbance curve of a sunscreen is obtained by measuring the transmitted UV spectrum of the substrate, with and without the sunscreen, and computing the negative logarithm of the transmission ratio at each wavelength interval. Product photostability is addressed by pre-irradiation of the sunscreen product with a UV dose corresponding to 1/3 the labeled sun protection factor (SPF) value.

Included in the report are recommendations based on the results of a round robbin evaluation of the proposed critical wavelength methodology involving six laboratories using four test sunscreen formulations with various substrates. You conclude that the critical wavelength method is a convenient, reproducible in vitro method for measuring the uniformity of sunscreen absorbance spectra across the UV spectrum for classifying products into broad UVA protection categories. You also urge the agency to consider these recommendations when developing a testing

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methodology to determine the UVA efficacy of sunscreen drug products.

The agency has the following specific comments on your protocol:

(1) On the top of page 4, it is stated that "a region of the substrate at least 1 cm^2 in area will be measured (spectrometer)" or "5 individual regions of the substrate at least 0.25 cm^2 in area will be measured (spectroradiometer)." Please explain why the difference in instrumentation choice would influence the number of measurements taken or the size of the area measured.

(2) Under "Substrate" on page 4, please explain how the use of the quartz backing plate alleviates the incompatibility of the Transpore tape with certain vehicle ingredients and sunscreen application technique.

(3) Under "Pre-Irradiation of Sunscreen-Substrate Preparations" on page 6, please explain whether the minimal erythemal dose (MED) of 1 J/cm^2 is intended to be a weighted or unweighted dose, or how this value (1 J/cm^2) was determined.

Feedback Meeting

At the January 27, 1999, public meeting (copy of meeting minutes enclosed), CTFA and CHPA agreed to provide the following additional data and information to the agency relative to UVA testing methodology and labeling:

- Rationale concerning the selection of the "critical wavelength" method over other in vitro UVA test methods (including the Diffey "ratio" method)
- Response to the observation that products with significantly different absorption spectra can have similar "critical wavelength" values
- Sunscreen product absorbancy/transmission data requested for "ratio method" calculations
- Data relative to the determination of the "pre-irradiation" dose concerning the photostability modification to the "critical wavelength" method
- Data relative to the differential "wash-off" of ingredients during water immersion or sweating (i.e., differential changes to UVB and/or UVA absorption)

- "Diffuse reflectance" method, data/information; assessment and comparison with Diffey methods
- Information concerning the appropriate proportionality between UVB (relative to the SPF) and UVA absorption in sunscreen products
- Feedback regarding appropriate label claims

Conclusion

In accordance with your request, the agency is assessing the recommendations contained in the CTFA/CHPA Sunscreen Task Force submission. As discussed at the January 27th meeting, these recommendations are being considered in the context of other in vivo and in vitro testing methodologies and labeling approaches. Therefore, we believe that the submission of the above information is necessary for the determination of an appropriate testing methodology to assess the UVA protection potential of sunscreen drug products.

The requested information, along with your response to our specific comments on your protocol, should be submitted in three copies, identified with the docket and comment number shown at the beginning of this letter, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

We appreciate your cooperation in these matters and look forward to further dialogue in the future.

Sincerely yours,

Charles J. Ganley, MD
Director
Division of OTC Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

Meeting Date:	January 27, 1999
Time:	09:00 –10:30 A.M.
Location:	9201 Corporate Blvd. Rockville, MD Conference Room S-200
Subject:	Ultraviolet A (UVA) Radiation Test Methods for Sunscreen Drug Products
Type of Meeting:	Public Feedback Meeting
Meeting Chair:	John Lipnicki
Meeting Recorder:	Sakineh Walther

Food and Drug Administration Attendees:

Robert DeLap, Director, Office of Drug Evaluation V (ODE-V), HFD-105
Debra Bowen, Deputy Director, ODE-V, HFD-105
Mary Jane Walling, Associate Director, ODE-V, HFD-105
Jonathan Wilkin, Division Director, Division of Dermatology and Dental Drug Products, HFD-540
Linda Katz, M.D., Deputy Director, Division of OTC Drug Products, HFD-560
Steve Aurecchia, Medical Officer, HFD-560
Gerald Rachanow, Regulatory Counsel, HFD-560
John Lipnicki, Interdisciplinary Scientist Team Leader, HFD-560
Donald Dobbs, Interdisciplinary Scientist, HFD-560
Kay Freeman, Interdisciplinary Scientist, HFD-560
Abby Jacobs, Pharmacologist/Toxicologist Team Leader, HFD-540
Paul Brown, Toxicologist, HFD-540
Sharon Miller, Optical Engineer, Center for Devices and Radiological Health/Office of Science and Technology, HFZ-134
Jim Timper, Chemist, Office of New Drug Chemistry, HFD-520

Cosmetic, Toiletry, and Fragrance Association (CTFA)/Nonprescription Drug Manufacturers Association (NDMA) Attendees:

Tom Donegan, Vice President-Legal & General Counsel, CTFA
Gerald McEwen, Vice President, Science, CTFA
Eve Bachrach, Senior Vice President, General Counsel, NDMA
Myra Barker, Chief Scientific Officer, Mary Kay Holding Corp., Chairperson, CTFA/NDMA Sunscreen Task Force

Other Attendees:

Kathleen Walker, Program Manager, Clinical, Avon Products
Ken Marenus, Vice President, Bio-Research
Sybil Mead, F-D-C Reports
Javier Avalos, Research Leader, Jergens
Marjorie McTeman, Director, Regulatory Affairs, Johnson and Johnson
Curtis Cole, Manager, Product Development, Johnson and Johnson
Kevin Carr, Director, Product Development, Labsphere
Chris Corbett, Assistant General Counsel, L' Oreal/Cosmair
Cheryl Sanzare, Director Regulatory Affairs, L' Oreal/Cosmair
Mark Rosengarten, Director, Regulatory Affairs, Playtex
Tim Elliott, Manager, Regulatory Affairs, Procter and Gamble
Chris Armstrong, Regulatory Manager, Procter and Gamble
J.F. Nash, Senior Scientist, Procter and Gamble
Patricia Agin, Director, Photobiology, Schering-Plough
Mark Mitchnick, Chief Executive Officer, SunSmart

Meeting Objective:

Public feedback meeting to discuss UVA radiation testing methodology for sunscreen drug products.

Background:

This meeting was requested by the CTFA for the purpose of obtaining feedback to the April 9, 1996, CTFA/NDMA Joint Sunscreen Task Force submission titled, "Critical Wavelength Determination for the Evaluation of the UVA Efficacy of Sunscreen Products" (filed as Comment RPT9 under Docket No. 78N-0038 in the Dockets Management Branch).

Discussion Points:

- Based upon what we know today, how do we get appropriately tested and labeled products out there for consumers?

- What is known and what are the uncertainties concerning sunscreen product absorption at specific wavelengths (and amount of absorption) in relation to protection from various types of photodamage (and what that damage may be)?

- What are the limitations of in vivo methods, considering the uncertainties with respect to UVA photodamage action spectra and uncertainty regarding the clinical significance of endpoints (e.g., immediate or prolonged pigment darkening)?

- In vivo UVA test methods
  - should have clinically relevant endpoints
  - should provide information which does not simply mirror the results of SPF testing (e.g., erythema, short wavelength UVA)
  - may provide more clinically meaningful information if the test is performed in humans

- In vitro test methods
  - discussed disadvantages inherent to in vitro methods
  - discussed advantages of the "Diffey method"

- In lieu of an accepted, validated in vivo method that could demonstrate clinical benefit using clinical endpoints, a potential method should demonstrate an acceptable minimum level of protection across the entire UVB/UVA spectrum.

- Discussed concerns regarding the CTFA/NDMA "critical wavelength" submission of 4-9-96
  - products with significantly different absorption spectra can have similar "critical wavelength" values
  - uncertain what the clinical significance of the "critical wavelength" may be

- Suggestions for possible improvements to the "critical wavelength" method (if the significance of the "critical wavelength" method can be adequately established); industry input requested
  - modification of the "Boots method" (e.g., UVB/UVA-I vs UVB/UVA-II)
  - sunscreen product absorbancy/transmission data requested for "ratio method" calculations
  - request for data relative to determination of the "pre-irradiation" dose
  - request for data relative to differential "wash-off" of ingredients
  - "diffuse reflectance" method – data/information requested

- Consideration of the proportionality between levels of UVB to UVA blockage in sunscreen products (e.g., should high SPF products also be expected to offer relatively high UVA protection?)

- Applicable test data must be relevant to product labeling
  - "broad spectrum" types of labeling claims should be supported by evidence that the product provides significant and meaningful absorption across the entire UVB/UVA spectrum
  - claims concerning the prevention of skin cancer or photoaging may be appropriate in the context of a sun avoidance program that includes the use of sunscreens and protective clothing
  - feedback requested relative to appropriate label claims

- Industry concerns
  - educational information versus required product information on labels
  - validation and reproducibility of test methods
  - acceptance of multiple test methods
  - pending sunscreen active ingredient petitions
  - appropriate labeling for everyday use products (e.g., drug-cosmetics)

Action Items:

- Written agency feedback to the 1996 CTFA/NDMA critical wavelength submission will be provided to CTFA

- CTFA/NDMA will provide the following additional data/information; a timeline will be submitted within the next two weeks for the submission of this information:
  - rationale concerning the selection of the "critical wavelength" method over other in vitro UVA test methods (including the Diffey "ratio" method)
  - response to the observation that products with significantly different absorption spectra can have similar "critical wavelength" values
  - sunscreen product absorbancy/transmission data requested for "ratio method" calculations
  - data relative to the determination of the "pre-irradiation" dose concerning the photostability modification to the "critical wavelength" method
  - data relative to the differential "wash-off" of ingredients during water immersion or sweating (i.e., differential changes to UVB and/or UVA absorption)
  - "diffuse reflectance" method – data/information – assessment and comparison with Diffey methods
  - information concerning the appropriate proportionality between UVB (relative to the SPF) and UVA absorption in sunscreen products
  - feedback regarding appropriate label claims

Sakineh H Walther

Sakineh Walther, Meeting Recorder

John Lipnicki, Chair Concurrence

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 7-16-99

FROM: Director
Division of OTC Drug Products, HFD-560

SUBJECT: Material for Docket No. 78N-0038

TO: Dockets Management Branch, HFA-305

[X] The attached material should be placed on public display under the above referenced Docket No.

[X] This material should be cross-referenced to Comment No. RPT 9

Charles J. Ganley, M.D.

Attachment